REMARKS

Reconsideration is respectfully requested in view of the above amendments and following remarks. The specification has been amended to recite vincristine and vinblastine as general names rather than registered trademarks. In addition, the general names of registered trademarks Navelbine®, Taxol® and Taxotere® have been added. Claims 1, 9 and 15-16 are hereby amended. Claims 1 and 9 have been amended to incorporate the limitation of at least one other antitumor agent selected from the group consisting of platinum compounds, topoisomerase acting agents, microtubule acting agents and antitumor antibiotics, which is supported for example by page 4, lines 8-13 and claim 5. Claims 15-16 have been amended editorially. Claims 5-8, 10-14 and 17-23 are canceled without prejudice or disclaimer. Claims 24-27 are new. Claims 24-26 are supported for example by page 11, lines 7-30 and page 12, lines 1-19. Claim 27 is an independent method claim generally corresponding to previous claim 13 and supported by page 15, lines 12-30 and page 16, lines 1-9. Claims 1-4, 9, 15-16, and 24-27 are pending.

Claim rejections - 35 U.S.C. § 112

Claim 1 is rejected under 35 U.S.C. 112(a), second paragraph, as being indefinite for failing to claim the subject matter of the present invention. Claim 1 has been amended editorially, taking the issues noted in the rejection into account. Applicants respectfully submit that claim 1 is definite.

Favorable reconsideration and withdrawal of the rejection are respectfully requested.

Claim rejections - 35 U.S.C. § 102

Claims 1 (in part) and 2-4 are rejected under 35 U.S.C. 102(b) as being anticipated by Hidaka et al. (U.S. Patent No. 5,972,976). The rejection is rendered moot as claim 5, whose limitations are now present in claim 1, was not rejected. Applicants do not concede the correctness of the rejection.

Favorable reconsideration and withdrawal of the rejection are respectfully requested.

Claim rejections - 35 U.S.C. § 103

Claims 1-19 are rejected under 35 U.S.C. 103(a) as obvious over Hidaka, in view of Goodman and Gilman, The Pharmacological Basis of therapeutics and Ragaz et al., The New England J. of Med. Applicants respectfully traverse this rejection.

Claim 1 requires the composition to include both formula (I) and at least one other antitumor agent selected from the group consisting of platinum compounds, topoisomerase acting agents, microtubule acting agents and antitumor antibiotics (see page 4, lines 8-13 for example). By administering formula (I) in the presence of another antitumor agent listed above, the survival rate T/C (%) is significantly improved, which is supported for example by Table 1. Moreover, the combined administration exerts potent inhibitory activity on cell growth as compared to a single administration of the respective compounds (see Figs. 2A and 2B and page 20, lines 5-12 for example).

Clinically, an antitumor agent is not used alone. However, it is necessary to select a combination of antitumor agents with low cross resistance and, more

importantly, with low or no enhancement of toxicity in order to achieve significant improvement in the survival rate. By combining formula (I) and another antitumor agent(s) selected from the group that cause a very low frequency of cross resistance, the present invention enjoys enhanced antitumor effects and reduced toxicity. In fact, according to this combined administration, the T/C value becomes over 3 times greater than in the case where the agents are administered alone (compare Compound 2 and CDDP alone, and Compound 2 and CDDP combined in Table 1). Hidaka fails to teach a pharmaceutical composition comprising formula (I) and another antitumor agent that causes a very low frequency of cross resistance. Further, Hidaka used compounds of formula (I) for avoiding adverse reactions with anticancer hormones (see page 2, lines 39-40). Nothing in Hidaka or any of the other references suggests that improved survival rate could be achieved by combining formula (I) with other antitumor agents.

Goodman discloses that "[d]rugs are generally more effective in combination and may be synergistic through biochemical interactions." However, there are many antitumor agents that could be combined. Unless an appropriate combination is selected, even if the antitumor effect is increased, the toxicity of the agents may be enhanced. Goodman fails to teach or suggest any particular combination that would be reasonably expected to improve the survival rate, and thus represents nothing more than invitation to experiment.

The present invention is based on the finding that formula (I) did not show cross resistance to cell lines resistant to typical antitumor agents such as Adriamycin®, cisplatin or Taxol® (see page 10, lines 23-26 for example). Further, an unexpected lowering of toxicity of respective agents was observed by combining formula (I) with

cisplatin, as show in Table 1, which compares data indicating significant improvements in the survival rate by the present invention. For example, when the respective compounds were administered alone, T/C values were between 125 and 170, and the survival rate on day 5 was not observed for either drug. However, when these drugs were administered in combination, the combined administration group showed T/C values of >500, and furthermore, survival rate of 5/6 was observed even on day 50. In view of these findings, Applicants submit that the present invention provides benefits that would have been unexpected to one of ordinary skill.

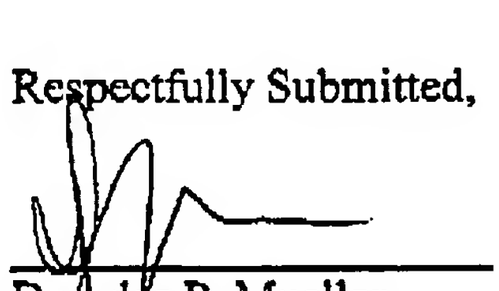
Ragaz is directed to radiotherapy. This reference is rendered moot as claims 10-12 were canceled.

Favorable reconsideration and withdrawal of the rejection are respectfully requested.

In view of the above, favorable reconsideration in the form of a notice of allowance is requested. Any questions or concerns regarding this communication can be directed to the attorney-of-record, Douglas P. Mueller, Reg. No. 30,300, at (612) 455.3804.

Dated: February 9, 2006

Respectfully Submitted,



Douglas P. Mueller
Reg. No.: 30,300
Hamre, Schumann, Mueller & Larson, P.C.
225 South Sixth Street
Suite 2650
Minneapolis, MN 55402
612.455.3800

DPM/ym